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PH/5-30706A/C1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

DAVID JOHN NEVILL, ANDREAS ZOSCHKE

and ANDREAS STEHLI

SERIAL NO. 09/852 484

Filed: May 10, 2001

For: Herbicidal Compositions

Group Art Unit: 1616

Examiner: S. Mark Clardy

Commissioner of Patents and Trademarks

Washington, D.C. 20231

DECLARATION UNDER RULE 132

I, Daniel North, a citizen of the United Kingdom, residing in CH-4104 Oberwil, Baselland, Switzerland, hereby declare:

CREDENTIALS

1. That I was awarded the degree of a B.Sc. in Biological Sciences by the Birkbeck College, University of London in 1998;
2. That I was employed by ZENECA and now SYNGENTA AG, Basel, Switzerland as a Biologist since 1993 and presently hold the position of a Team Leader in the field of crop protection, herbicides;
3. That I have been engaged in research work in the field of weed control for ZENECA and now SYNGENTA AG since 2001;
4. That prior to my employment with ZENECA and now SYNGENTA AG I was employed by SHELL as a Biologist from 1991 to 1993 in the "Biology Department" and that I was engaged in biological research in the field of entomology;

BIOLOGICAL TEST PROCEDURES

5. That the following tests were carried out under my supervision in a greenhouse in Stein/Switzerland to determine the relative herbicidal actions of the following compounds and mixtures within the scope of instant application:

Compounds and mixtures	Rate [g/ha]	Formulated as:
Compound of the formula A	12	EC100
(S)-Metolachlor	250	EC960
Atrazine	250	SC500
Nicosulfuron	15	SC040
Mesotrione	75	SC100
(S)-Metolachlor + Atrazine	250 + 250	
(S)-Metolachlor + Mesotrione	250 + 75	
Compound of the formula A + (S)-Metolachlor	12 + 250	
Compound of the formula A + Atrazine	12 + 250	
Compound of the formula A + Nicosulfuron	12 + 15	
Compound of the formula A + Mesotrione	12 + 75	
Compound of the formula A + (S)-Metolachlor + Atrazine	12 + 250 + 250	
Compound of the formula A + (S)-Metolachlor + Mesotrione	12 + 250 + 75	

These compounds were formulated as Standard Formulations EC100 and EC960 for Compound of the formula A and (S)-Metolachlor, respectively, and SC500, SC040 and SC100 for Atrazine, Nicosulfuron and Mesotrione, respectively in the presence of 0.2 % of the additive X-77. The formulated compounds were dispersed in water (500 l/ha), diluted to spraying concentrations and sprayed with a linear moving track spray system individually as well as in mixture as comparative post-emergence tests on the following plants:

Maize "DK-554 WT" (wild-type maize)

Maize "MHT 152 GMO" (GMO Maize)

Echinochloa crus-galli

The test method employed was as follows:

Post-emergence test:

The test plants are raised in plastic pots containing standard soil. At the 3-6 leaf-stage, the plants are sprayed with an aqueous suspension of the individual test-compounds corresponding to rates of application of 12 g ai/ha for Compound of the formula A, 15 g ai/ha for Nicosulfuron, 75 g ai/ha for Mesotrione and 250 g ai/ha for (S)-Metolachlor and Atrazine, and of the 2- and 3-components mixtures thereof with the corresponding rates of application for the single components as mentioned above (500 l water/ha) and transferred to the greenhouse for further cultivation under

optimal conditions. The evaluation takes place after 9 days, whereby the rating scale of 0-100 % is employed, where 0 % represents no herbicidal effect and 100 % equates to total damage when compared to the untreated controls;

6. That the following results as mean values of 4 plants per species were obtained:

Table 1: Post-emergence action of the individual components of compound of the formula A (12 g /ha), (S)-Metolachlor (250 g/ha), Atrazine (250 g/ha), Nicosulfuron (15 g/ha) and Mesotrione (75 g/ha), and of the mixture components (S)-Metolachlor + Atrazine (250 + 250 g/ha) and (S)-Metolachlor + Mesotrione (250 + 75 g/ha). Measured phytotoxic action in a rating scale of 0-100 % 9 days after application.

Plant tested:		Rate [g ai/ha]	Maize DK-554 WT		Maize MHT 152		Echinochloa crus-galli	
Comp. 1	Comp. 2							
Compd. of the formula A		12	60		20		70	
(S)-Metolachlor		250	0		0		0	
Atrazine		250	0		0		30	
Nicosulfuron		15	0		0		40	
Mesotrione		75	0		10		50	
(S)-Metolachlor	+ Atrazine	250+250	0		10		60	
(S)-Metolachlor	+ Mesotrione	250+75	0		20		30	

Table 2: Post-emergence action of the mixture components with compound of formula A 12 g/ha, and (S)-Metolachlor 250 g/ha, Atrazine 250 g/ha, Nicosulfuron 15 g/ha or Mesotrione 75 g/ha, or (S)-Metolachlor + Atrazine 250 + 250 g/ha or (S)-Metolachlor + Mesotrione 250 +75 g/ha. Measured phytotoxic action in a rating scale of 0-100 % 9 days after application.

Plant tested:				Maize DK-554 WT		Maize MHT 152		Echinochloa crus-galli	
Mixture component for Compound of the formula A 12 g/ha:			Rate [g ai/ha]	Obs	Exp	Obs	Exp	Obs	Exp
(S)-Metolachlor			250	90	60	0	20	95	70
Atrazine			250	70	60	0	20	80	79
Nicosulfuron			15	80	60	0	20	95	82
Mesotrione			75	90	60	0	28	98	85
(S)-Metolachlor	+	Atrazine	250+250	95	60	10	20	95	79
(S)-Metolachlor	+	Mesotrione	250+75	95	60	10	28	98	85

In above Table 2 'Obs' means observed phytotoxic action.

In above Table 2 'Exp' means expected (calculated) phytotoxic action according to Colby formula.

Observation: From the data of above Table 1 it can be derived that the protoporphyrinogen-oxidase-inhibiting herbicide Compound of the formula A taken individually has medium phytotoxic activity against wild-type maize DK-554 WT (rating 60 %) and strong, although economically inefficient herbicidal activity against *Echinochloa crus-galli* (rating 70 %), and only weak herbicidal activity against the maize MHT 152 made resistant to protoporphyrinogen-oxidase inhibitors (rating 20 %) at the measured rate of application of 12 g/ha.

On the other side, the individual co-herbicides (S)-Metolachlor, Atrazine, Nicosulfuron and Mesotrione as well as the 2-component mixtures (S)-Metolachlor + Atrazine and (S)-Metolachlor + Mesotrione show no phytotoxic activity at all against the tested wild-type maize DK-554 WT, none or weak phytotoxic activity against the GMO maize MHT 152 (ratings 0-20 %) and none to medium herbicidal activity against *Echinochloa crus-galli* (ratings 0-60 %) at the employed application rates of 15 g, 75 g and 250 g/ha, and 250 + 250 g/ha and 250 + 75 g/ha, respectively.

From the data of the Table 2 it can be derived that the mixture components with Compound of formula A (12 g/ha) and the listed co-herbicides taken individually as well as the 2-components mixtures of co-herbicides result in a surprisingly homogeneous and clear herbicidal spectrum against the plants tested, namely in a significantly better herbicidal activity against *Echinochloa crus-galli* observed (Obs) than could be expected (Exp) according to the Colby formula at the measured rates of application i.e. a clear-cut synergistic enhancement in weed control can be observed. Only the mixture component with Compound of formula A + Atrazine gives a marginal improvement from 79 % (expected) to 80 % (observed) phytotoxicity against *Echinochloa* at the measured rate of application.

A synergistic effect of instant mixture components with Compound of the formula A and the listed single co-herbicides as well as the 2-components mixtures of co-herbicides in Table 2 is observed against the wild-type maize DK-554 WT too, as expected. The overall synergistic effect of between 10-35 % however is even more pronounced against said wild-type maize compared to the overall synergistic effect of between 1-25 % against the tested weed *Echinochloa*.

Surprisingly now, the inventive 2-components mixture with Compound of the formula A and the listed single co-herbicides on the one side result in no phytotoxic activity at all against the genetically engineered (GMO) maize MHT 152 (rating 0 %) and on the other side the 3-components mixture with Compound of the formula A and the 2-components mixtures of co-herbicides result in a weak phytotoxic activity (rating 10 %) only against said maize MHT 152 at the measured application rates. The expected phytotoxicity according to the Colby formula on maize MHT 152 would be in the range of 20 to 28 %. This is significantly higher than the observed weak phytotoxic activity of

10 % obtained with the 3-components system of Compound of the formula A + (S)-Metolachlor + Atrazine and Compound of the formula A + (S)-Metolachlor + Mesotrione on said genetically engineered maize MHT 152.

These results are indicative of a clear-cut synergistic effect on the weed *Echinochloa crus-galli* in addition to an antagonistic effect against the maize MHT 152 (but not against wild-type maize DK-554 WT) for all the 2- and 3-components mixtures as listed in Table 2.

It is especially unexpected that additional to the synergistic enhancement in weed control a synergistic enhancement of GMO crop selectivity can be observed too. This synergistic enhancement of GMO crop selectivity results in an additional increase in the safety margin with regard to the crop plants i.e. a broader flexibility for the application of the presently claimed compositions.

CONCLUSIONS

7. These results are indicative of

- (a) the excellent overall synergistic effect in connection with the herbicidal performance of the inventive compositions relative to the single compounds, and
- (b) a synergistic enhancement in connection with GMO crop selectivity.

8. This synergistic improvement of GMO crop tolerance with at the same time the synergistic improvement of herbicidal activity is surprising because in the test data the performance of the inventive compositions comprising Compound of the formula A and the single co-herbicides (S)-Metolachlor, Atrazine, Nicosulfuron or Mesotrione, or the 2-components mixtures of (S)-Metolachlor + Atrazine or (S)-Metolachlor + Mesotrione

- (a) post-emergent at the measured rates of application of the compositions, and
- (b) against 1 weed and 2 crop species

is clearly superior relative to the performance of said compounds taken separately at the same rates as in said compositions.

The compositions result in very strong herbicidal activity of the tested weed species with at the same time improved selectivity of the GMO crop plant maize.

This demonstrates a clear twofold synergistic enhancement in

a) weed control, and

b) GMO crop selectivity, which is surprising and unobvious and which is in its magnitude recognized by the one skilled in the art.

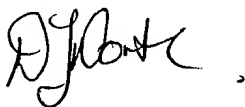
9. This superior performance is important because it allows reduced application rates of the individual compounds while achieving a constant good selective herbicidal action. On the other hand, the inventive mixtures achieve a high degree of weed control even where the individual compounds of the mixtures have become ineffective in the region of very low application rates.

This results in an additional increase in the safety margin with regard to the GMO crops.

FINAL STATEMENT

I, Daniel North, declare further that all statements made herein of personal knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Signed this 13 day of February, 2002.

A handwritten signature in black ink, appearing to read "D. North", is written below the signature line.